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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,482	12/12/2005	Frans Eduard Janssens	PRD2077USPCT1	3160

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EXAMINER	
BAEK, BONG-SOOK	
ART UNIT	PAPER NUMBER
1614	

NOTIFICATION DATE	DELIVERY MODE
08/25/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/560,482	JANSSENS ET AL.	
	Examiner	Art Unit	
	BONG-SOOK BAEK	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,9-14 and 21-26* is/are pending in the application.

4a) Of the above claim(s) *9 and 21-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 10-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of claims

The amendment filed on June 29, 2010 is acknowledged. Claims 2-8 and 15-20 have been canceled and claims 9 and 21-26 have been withdrawn. Claims 1 and 10-14 are under examination in the instant office action.

Applicants' arguments, filed on June 29, 2010, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application. Responses are limited to Applicants' arguments relevant to either reiterated or newly applied rejections.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1 and 10-14 are rejected under 35 U.S.C. § 103(a) as being unpatentable over US patent 5,880,132 (issue date: 3/9/1999) in view of US patent 6,197,772 B1.

US patent 5,880,132 teaches a pharmaceutical composition comprising a tachykinin antagonist in paricular an NK_1 receptor antagonist and an opioid analgesic, together with at least one pharmaceutically acceptable carrier or excipient for the treatment or prevention of pain or nociception (abstract; column 1, lines 7-10; and column 2, lines 33-36). US patent 5,880,132 defines that the term opioid is generally accepted to refer in a generic sense to all drugs, natural or systhetic with morphone-like action and lists fentanyl as a preferred opioid analgesic (column 1, line 52-56, column 26, lines 23-29, claim 2). US patent 5,880,132 further teaches that the composition may be present as a combined preparation for simultaneous, separate or sequential use for the treatment or prevention of pain and formulated into unit dosage forms for oral administration (column 2, lines 42-46, column 26, line 56-60, and claim 4). This teaching reads on the limitations recited in instant claims 11 and 14. In addition, the reference teaches that respiratory depression is a common side effect associated with opioid analgesic usage (column 2, lines 1-5) and that the composition is possible to treat pain with a sub-maximal dose of an opioid analgesic thereby reducing the likelihood of side-effects associated with opioid analgesic usage such as respiratory depression by the use of a combination of a tachykinin antagonist and an opoid analgesic (column 2, line 61-column 3, line 3). Furthermore, it teaches that the tachykinin antagonists of use may be any tachykinin antagonist known from the art and preferably, the

tachykinin antagonist is an NK-1 or NK-2 receptor antagonist, especially an NK-1 receptor antagonist (column 3, lines 7-10).

The reference differs from the instant claims insofar as it does not teach the elected species, (+)-(B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N-(2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid.

US patent 6,197,772 B1 teaches (+)-(B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid as tachykinin antagonist (NK_1 receptor antagonist) (column 1, lines 9-14, column 1, line 44-column 4, line 23; column 7, line 39-column 8, line 5; claims 1-3), which can be used for the treatment of pain, emesis, or asthma (column 18, lines 33-44). Also, US patent 6,197,772 B1 teaches that the compound may be formulated into various pharmaceutical forms for administration purposes such as oral administration (column 18, line 45-56). In addition, it discloses that an effective therapeutic daily amount is from about 0.001 mg/kg to about 40 mg/kg body weight, more preferably from about 0.01 mg/kg to about 5 mg/kg body weight, wherein the disclosed dosage range is identical to the dosage range used for reducing respiratory depression in the instant specification (p18, line 9-12 and p54, example C4). Thus, the effective therapeutic daily amount of (+)-(B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic taught by US patent 6,197,772 B1 reads on "an amount effective to reduce the respiratory depression caused by the administration of an opioid analgesic" recited in the instant claim 1 .

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the compound of US patent 6,197,772 B1 for the combination with

fentanyl as taught by US patent 5,880,132 in the treatment of pain since US patent 6,197,772 B1 teaches (+)-(B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N-(2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid as tachykinin antagonist and US patent 5,880,132 already suggests that any tachykinin antagonist known from the art can be used for the combination with an opioid analgesic, wherein the combination is beneficial for reducing opioid analgesic-associated side-effects such as respiratory depression. Furthermore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to substitute one tachykinin antagonist with another tachykinin antagonist for the combination with an opioid analgesic as taught by US patent 5,880,132 since the skilled artisan would have been able to carry out such a substitution and the results (i.e., treating pain while reducing opioid analgesic-associated side-effects such as respiratory depression) were reasonably predictable. Furthermore, one of ordinary skill in the art at the time the invention was made would have reasoned to use an effective amount of (+)-(B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N-(2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid as taught by US patent 6,197,772 B1 for making a combination with an opioid analgesic as taught by US patent 5,880,132. When the disclosed effective amount of (+)-(B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid is used in combination with an opioid analgesic as taught by US patent 5,880,132, reducing respiratory depression would be an expected outcome. It is noted that products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant

discloses and/or claims are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Response to Applicants' arguments:

Applicants argued that US 5,880,132 does not teach or suggest any means or compounds for overcoming of counteracting the respiratory depression associated with opioid analgesics, but rather teaches decreasing opioid dosages as a means of avoiding respiratory depression and other adverse effects and compensating for the decreased efficacy with a tachykinin antagonist. In response to this argument, US patent 5,880,132 already teaches the use of a tachykinin antagonist in combination with an opoid analgesic makes it possiboe to use a sub-maximal dose of an opioid analgesic in the treatemnt of pain, thereby reducing the likelihood of side-effects associated with opioid analgesic usage such as respiratory depression. Thus, US patent 5,880,132 does suggest a means or compounds (i.e., tachykinin antagonist) for overcoming of counteracting the respiratory depression associated with opioid analgesics. In addition, US patent 6,197,772 B1 teaches the same compound as a tachykinin antagonist and the same effective therapeutic daily amount as the instant invention, thus when the effective amount of (+)-(B)-trans-4-[1-[3,5-bis (trifluoromethy) benzoyl]-2-(phenymethy)-4-piperidiny]-N- (2,6-dimethylphenyl)-l-piperazine acetamide, (L)-malic acid as taught by US patent 6,197,772 B1 is used in combination with an opioid analgesic as taught by US patent 5,880,132, reducing respiratory depression necessarily happens. It is noted that products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims

are necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

As stated in the last office action, a skilled artisan would have been motivated to use the tachykinin antagonist of US patent 6,197,772 B1 in combination with an opioid analgesic such as fentanyl as taught by US patent 5,880,132 in the treatment of pain on the expectation that the combination would provide a composition useful for treating pain while minimizing opioid analgesic-associated side-effects such as respiratory depression. The claim language reciting the ability of the compound to reduce respiratory depression caused by the administration of the opioid analgesic constitutes nothing more than a property possessed by the compound used in the claimed composition. See MPEP § 2145(II) (indicating that arguing an otherwise obvious invention possess additional advantages or unrecognized properties cannot overcome a prima facie case of obviousness). Unless and until applicants can provide sufficient objective evidence of secondary indicia of nonobviousness commensurate in scope with the invention claimed, the rejections of record shall stand.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BONG-SOOK BAEK whose telephone number is 571-270-5863. The examiner can normally be reached 9:00-6:00 Monday-Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BONG-SOOK BAEK
Examiner, Art Unit 1614

Bbs

/Ardin Marschel/

Supervisory Patent Examiner, Art Unit 1614